

Sir:

II. Remarks

Claims 1-11 are pending.

1. Maintained Rejection under 35 U.S.C. § 112

A. Claim 10 has proper antecedent basis.

The Office has rejected Claim 10 under 35 U.S.C. 112 for insufficient antecedent basis for the limitation “Abu”. The Office suggests amending Claim 10 to depend from Claim 2 rather than Claim 3.

Applicant points out that as Claim 3 depends from Claim 2, Claim 3 necessarily contains all elements of Claim 2. The Office correctly acknowledges that Claim 10 could properly depend from Claim 2. As sufficient support for the limitation of “Abu” is present in Claim 2, all claims either directly or indirectly dependent from Claim 2 contain sufficient support for the limitation of “Abu”. As such, Applicant requests that the rejection be withdrawn.

2. New Rejection under 35 U.S.C. § 112

A. Claims 1 and 11 are definite and further have unambiguous and clear endpoints.

The Office has rejected Claims 1 and 11 under 35 U.S.C. § 112 “as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” The Office asserts that the “endpoint(s) of the claimed methods are ambiguous and unclear.”

On pages 4 and 5 of the specification, applicant describes the measured fluorescence polarization as an indicator of the amount of cleaved substrate in the mixture at the completion of the claimed method. The amount of cleaved substrate in the mixture at the completion of the claimed method is correlated to the activity of the protease of interest. As Claim 1 is a method of determining the activity of a protease, and

Claim 11 is a method of identifying compounds which inhibit a protease, the measurement of the polarization of the fluorescence is a definite endpoint. As such, applicant requests that the rejection be withdrawn.

3. Rejections under 35 U.S.C. § 103

A. Claims 1-11 are non-obvious.

The Office has rejected Claims 1-11 under 35 U.S.C. 103(a) as being obvious over Heath et al. (U.S. Pat. No. 5,235,039), Bromberg (U.S. Pat. No. 4,203,670), and Maeda (Analytical Biochemistry 1979) in view of Welch et al. (PNAS 1991) or Blakeslee et al. (Journal of Immunological Methods, 1976).

To establish a *prima-facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the teachings. Second, the references, when combined, must teach all the claim limitations. Third, there must be a reasonable expectation of success. See MPEP § 2143.

In the present case, the first criterion is not satisfied as impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the references. See MPEP 2142.

While applicant appreciates the Office's recognition that the development of a one step assay for the determination of activity herpes virus proteases represents an advance in the art, one of ordinary skill in the art, upon reading Heath, Bromberg, and Maeda in view of Welch and Blakeslee, would not be motivated, without impermissible hindsight, to combine their respective disclosures to practice the present invention.

Heath discloses a fluorescence detection method where the accuracy of the measurement of the polarization of fluorescence is a result of the isolation of the fluorescent entity from the solution. Heath does not disclose a peptidic substrate. Upon reading Heath, one of ordinary skill in the art would have no motivation to combine the disclosure of Heath with Bromberg, Maeda, Welch or Blakeslee.

Bromberg discloses a method for the measurement of the polarization of fluorescence in solution capable of producing in a reliable, repeatable and accurate manner, measurements of even extremely small polarization of low level fluorescence.

Bromberg does not disclose or suggest measuring the activity of a protease or a substrate capable of being bound to an anchor. Bromberg does not disclose a peptidic substrate. Upon reading Bromberg, one of ordinary skill in the art would have no motivation to combine the disclosure of Bromberg with Heath, Maeda, Welch or Blakeslee.

Maeda discloses the use of fluorescence polarization applied directly to the reaction mixture. Maeda does not disclose the applicability of his methods to proteases or substrates capable of being bound to an anchor. Maeda does not disclose the applicability of his methods to herpes protease assays. Upon reading Maeda, one of ordinary skill in the art would have no motivation to combine the disclosure of Maeda with Heath, Bromberg, Welch or Blakeslee.

As the disclosures of Heath, Bromberg and Maeda rely on substantially different techniques, fluorescence detection as opposed to measuring the polarization of fluorescence, applied to different phases of matter, isolated particles as opposed to solutions or mixtures, one of ordinary skill in the art would not be motivated to combine the disclosures.

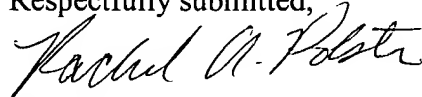
Welch *et al.* discloses the herpes virus proteinase assembling, its gene, putative active site domain and cleavage site. Welch discloses techniques applicable to a limited number of compounds of interest, as opposed to the high-throughput capability of the present invention. Welch does not disclose attaching a fluorophore to a substrate or substrates capable of being bound to an anchor, as required by the present invention. The protein screening assay disclosed in Welch relies on gel electrophoresis with ^{125}I -labeling. Welch also does not disclose either the method of fluorescence detection or measuring the polarization of fluorescence. Applicant states on page 2 of the present invention that

Initial assays used in the characterization of herpesvirus proteases have been based on electrophoretic separation of products. See EP 514,830. Such method is impractical for screening large numbers of enzymatic inhibitors. An assay which allows for quantitative kinetic characterization of the interaction of the inhibitors with herpesvirus proteases is more preferred.

As the disclosure in Welch relies on fundamentally different principles, there is no motivation for one of ordinary skill in the art to combine Welch with Heath, Bromberg or Maeda.

Thus, the disclosures of Heath, Bromberg, and Maeda in view of Welch and Blakeslee fail to satisfy the first criteria necessary for establishing a *prima-facie* case of obviousness. Because no *prima-facie* case of obviousness can be made, withdrawal of the rejection the present application under 35 U.S.C. § 103 is respectfully requested. Therefore, the present application is believed to be in condition for allowance.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Rachel A. Polster".

Rachel Polster

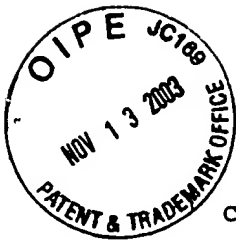
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CERTIFICATE OF MAILING BY FIRST-CLASS MAIL (37 CFR 1.8)

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Date of Deposit: November 10, 2003

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